UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,071	05/08/2001	Ann Marie Schmidt	0575/55424-Z/JPW/SHS/MVM	3248

7590 04/10/2003

John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	12

DATE MAILED: 04/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/851,071	Applicant(s) SCHMIDT ET AL.	
	Examiner Sumesh Kaushal Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-38* is/are pending in the application.

4a) Of the above claim(s) *22-32 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-21,33-35,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 01/21/03 has been acknowledged.

Claims 17-38 are pending
Claims 22-32 and 36 are withdrawn from further consideration (nonelected invention).
Claims 17-21, 33-35 and 37-38 are examined in this office action.

► *Applicants are advised to follow Amendment Practice under revised 37 CFR §1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). Each amendment document that includes a change to an existing claim, or submission of a new claim,* ***must include a complete listing of all claims*** *in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.*

Election/Restrictions

1. Applicant's election with traverse of Group III (claims 17-21, 33-35 AND 37-38, wherein the elected species is "a small molecule") in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the inventions of group I-IV are not distinct and there is no serious burden to examine these groups as one single invention (response page 5, para 3). The applicant argues that invention of group III relates to invention of groups I, II and IV, since all group rely upon the ability of an agent to inhibit RAGE/ligand as part of their design, operation and effect. In support applicant cited the instant specification that teaches that RAGE/amphoterin interaction interfere with the ability of tumors to compromise the integrity of local environment (response page 6, para.2). The applicant maintains that there would not be a serious burden to examine all

groups as one single invention. This is not found persuasive because the scope of invention as claimed is not limited to RAGE/amphoterin interaction (see Groups I, II and III). The polypeptides and antibodies of group I and II are structurally and functionally distinct compounds wherein the search of one would not lead to the finding of other and would not further lead to the subject matter related to RAGE/amphoterin interaction. Furthermore, search of Group II requires the search of SEQ ID NO:3, 4, 5 and 6 which is not required for the search of group I and visa versa. In addition, the invention of Group III requires the search of an agent that inhibits the interaction between the tumor cell and an extracellular matrix molecule like αVβV, αVβIII, αIβII integrins, whereas Group IV only requires an agent that inhibits the binding of RAGE/amphoterin interaction. Searching αVβV, αVβIII, αIβII integrins would not lead to the finding of a subject matter related to RAGE/amphoterin interaction. Thus the examination of these groups as one single invention clearly imposes a serious burden on the office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 22-32 and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 17-21, 33-34 and 37-38 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Chintala et al (Cancer Lett 103:21-208, 1996).

The invention as claimed is drawn to a method for evaluating the ability of an agent to inhibit tumor invasion in a local cellular environment. The scope of candidate agent encompasses a small molecule, which inhibits the interaction of tumor cell with an extra cellular matrix.

The cited art teaches a method for evaluating the ability of an agent to inhibit tumor invasion in a tumor cell culture (page 201 abstract). The invasive ability of the SNB19 and U251 human glioma cells in-vitro was measured by the invasion of cells through metrigel in 48-well microchemotaxis chamber (page 203, col.1 para.1; page 204, fig-2; page 205, fig 3, 4; page 207, fig-7). The cited art further teaches the evaluation of candidate agents that inhibit an interaction between the tumor cell and an extracellular matrix molecule like collagen, laminin, fibronectin and $\alpha 3\beta I$ integrin (page 201-202; page 204, fig-2; page 205, fig 3, 4, page 207, fig-7). The cited art further teaches that integrins are transmembrane hetrodimeric glycoproteins comprised of an $\alpha(16)$ and $\beta(8)$ subunits, which can combine to form at least 20 receptor types (page 201-202). In addition cited art teaches RGD inhibits the interaction of glioblstoma cell lines with fibronectin in a dose dependent fashion (page 203, col.2 para.2). Thus the cited art clearly teaches the

method for evaluating the ability of an agent to inhibit tumor invasion and a composition comprising the agent identified using the method as claimed.

3. Claims 17-21, 33-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Softer et al (PNAS 89:1557-1561, 1992).

The invention as claimed is drawn to a method for evaluating the ability of an agent to inhibit tumor invasion in a local cellular environment. The scope of candidate agent encompasses a small molecule, which inhibits the interaction of tumor cell with an extra cellular matrix, wherein the extracellular matrix is an αVβ3, αVβV or αIβII integrin.

The cited art teaches a method for evaluating the ability of an agent to inhibit tumor invasion using an in-vitro invasion assay in context with αVβ3 integrin (page 1557 abstract). The cited art explored the relationship between the function and expression of αVβ3 integrin in A375M human melanoma cells and ability of these cells to invade in-vitro by modulating αVβ3 integrin with either antibodies or its ligand vitronectin (page 1557 col.2 para.1). The cited art teaches that in-vitro invasion assay, wherein in the assay was performed in membrane invasion culture system (MICS) using polycarbonate filter containing 10μm pores coated with Metrigel. The cited art further teaches the determination of invasion potential of the treated and untreated tumor cells (page 1558, col.1 para.2, page 1559, fig-3). The cited art teaches that pretreatment of tumor cells with soluble vitronectin prior to assay resulted in increase in tumor cell invasion (page 1559, col.2 para.2). The cited art further teaches the A375M human melanoma cells express the αVβ3 integrin, wherein the αVβ3 integrin play an active role in

mediating the attachment of these cells to their substratum. The cited art further teaches that αVβ3 integrin is known to bind to number of Arg-Gly-Asp (RGD) containing proteins such as vitronectin, laminin and entacti/nidogen (page 1559, col.2 para.5). Thus the cited art clearly teaches the method for evaluating the ability of an agent to inhibit tumor invasion and a composition comprising the agent identified using the method as claimed.

4. Claims 37-38 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ruoslathi et al (US 5981478, 1999; filed 08/04/1994)[1].

The instant claims are drawn to a pharmaceutical composition that inhibits tumor invasion by inhibiting interaction between tumor cell and an extra cellular molecule like an integrin. Ruoslathi teaches a pharmaceutical composition comprising a RGD peptide that binds to αVβ3 and αVβ5 integrins in a pharmaceutically acceptable carrier (col.42 line 30). The cited art teaches that integrins mediates adhesion of cells to extracellular matrix (ECM) such as fibronectin, vitronectin collagens and laminin (col.1 line 10-20). The cited art further teaches that many integrins including α5β1, αVβ5, $\alpha_{11b}\beta3$ and αVβ3 are important in promoting cell attachment and recognize the amino acid sequence RGD (Arg-Gly-Asp) which is present in fibronectin and other adhesive proteins (col. 1, line 32-60). The cited art further teaches that peptides and protein fragments containing RGD sequences can be used to modulate the activity of RGD-recognizing integrins. The use of target RGD peptides permits target modulation and manipulation of cell adhesion and other integrin-mediated cellular events in various medical situations, including platelet aggregation, thrombosis, wound healing, osteoporosis, tissue repair

and tumor invasion (col.1 line 40-60). Furthermore the cited art teaches pharmaceutical composition comprising a peptide that binds to αVβ3 and αVβ5 integrins in a pharmaceutically acceptable carrier like an aqueous solution, oils or glycerol etc. (col.42 line 30, col.10 line 55-). Thus the invention as claimed is clearly anticipated by the cited prior art of record

5. Claims 37-38 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Pallandino et al (US 5767071, 1998; filed 06/07/1995)[2].

The instant claims are drawn to a pharmaceutical composition that inhibits tumor invasion by inhibiting interaction between tumor cell and an extra cellular molecule like an integrin. Palladino teaches a pharmaceutical composition comprising a non-RGd cyclic polyptide that binds to αVβ3 integrin receptor (col.41 line 1). The cited art teaches that αVβ3 integrin serves as a receptor for number of extracellular matrix proteins such as vitronectin, thrombospondin, von Willebrand factor, fibrinogen, fibrin and fibronectin (col.1 line 11-25). The cited art further teaches that αVβ3 integrin play a role in smooth muscle cell migration (col.2 line 7-24, col). The cited art further disclosed a cell migration assay to evaluate candidate compounds that inhibits smooth muscle cell migration (col.24, line 16-67). In addition the cited art teaches various pharmaceutical acceptable carriers like liposomes, inert diluents, ingestible tablets, or sterile aqueous solutions etc (col 15-19). Thus the invention as claimed is clearly anticipated by the cited prior art of record

[1, 2] **Note** (claims 37-38): Invention as claimed is a product by process, wherein the final product is indistinguishable from an agent that binds to αVβ3 or αVβ5 and inhibits interaction between tumor cell and an extracellular matrix.

The MPEP clearly states that the claims define the property rights provided by a patent, and thus require careful scrutiny. The goal of claim analysis is to identify the boundaries of the protection sought by the applicant and to understand how the claims relate to and define what the applicant has indicated is the invention. See *In re Hiniker Co., 150 F.3d 1362, 1369, 47 USPQ2d 1523, 1529 (Fed. Cir. 1998).* The subject matter of a properly construed claim is defined by the terms that limit its scope. As a general matter, the grammar and intended meaning of terms used in a claim will dictate whether the language limits the claim scope. Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation. The following are examples of language that may raise a question as to the limiting effect of the language in a claim: A) statements of intended use or field of use, B) "adapted to" or "adapted for" clauses, C) "wherein" clauses, or (D) "whereby" clauses. This list of examples is not intended to be exhaustive (*see MPEP 2106 Sec. II C).*

Furthermore, preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. *See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).* In addition, if the prior art structure is capable of performing the intended use, then it meets the claim. In a

claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. *See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963).* Thus the product as claimed is clearly anticipated by prior art of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 17-21 33-35 and 37-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim. For example, it is unclear what comprises "a local cellular environment" in this context.

Claim 21 is indefinite. The term "small molecule" in claim 21 is a relative term, which renders the claim indefinite. The term "small molecule" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In addition considering the claim limitation *"wherein the agent comprises a peptide, a petidomimetic, a nucleic acid, a synthetic organic molecule, an inorganic molecule, a*

carbohydrate, a lipid, an antibody or fragment thereof or a small molecule". Considering the instant disclosure it is not clear what encompasses a small molecule since an inorganic molecule like Ca^{2+} ion or an organic molecule like CH_4 or a single nucleotide base like A, T, G or C falls in the category of small molecules.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-8724 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
PATENT EXAMINER

SUMESH KAUSHAL
PATENT EXAMINER
PATENT EXAMINER